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RESEARCH ARTICLE

A OBSERVATIONAL STUDY ON COMPARING THE EFFICACY OF VITAMIN-E VERSUS MEADOXINE + L-ASPARAGINE IN HOSPITALIZED FATTY LIVER PATIENTS AT TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Fatty liver is a reversible condition in large vacuoles of triglycerides fat accumulates in the liver cells via the process of steatosis. It occurs in two forms, they are Alcoholic fatty liver and Non- alcoholic fatty liver. Alcoholic fatty liver is a condition in which excess fat is stored in the liver due to heavy alchol use. Non alcoholic fatty liver is a condition in which excess fat is stored in the liver This accumulation of fat is not caused by heavy alcoholic use.In this study our main main objective is to assess the efficacy and comparision between vit-E and metadoxine + L –Asparagine. In our study total 110 patients were included.out of 110,55 pa patients were prescribed with Vitamin E AND 55 patients were prescribed with metadoxine +L –Asparagine.To assess the efficacy of two drugs Fishers exact test was used.The drug vitamin E in 55 patients shows the reduced size of liver when compared to Metadoxine +L-Asparagine. Our study concludes that treatment of fatty liver with vitamin E is more effective when compared with treatment of Metadoxine +L-Asparagine.

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INTRODUCTION

Nonalcoholic liver disease disease (NAFLD), the foremost common explanation for chronic diseasein the western world, encompasses a histological spectrum of liver diseases starting fromsimple steatosis to nonalcoholic steatohepatitis (NASH), which may reach cirrhosis and liver cancer (Farrell, 2006). Within the US, the prevalence of NAFLD is estimated to be 17–33%and 5.7–17% for NASH (McCullough, 2006). The disease is closely related to obesity and diabetes and, due to their ongoing epidemics, the prevalence of NAFLD both in adults and youngsters islikely to extend over time and still become a significant public health burden. Currently, there's no definitive treatment for this disease. NASH is characterizedhistologically by the presence of hepatic steatosis, lobular inflammation, and hepatocytes ballooning (Sanyal *et al.,* 2011). Liver disorders are a principal cause of mortality and morbidity worldwide. Since 1980, mortality related to liver disorders has increased by 46%.1 In addition, non-alcoholic fatty liver disease (NAFLD) affects 20–30% of the population, and has become the most common liver disease worldwide. NAFLD is the process of lipid deposition within hepatocytes in the complete absence of excessive alcohol consumption or any otherknown cause of hepatic steatosis (Anderson *et al.,* 2015; Chen, 2020). The disease progresses from simple steatosis to steatohepatitis, with potential development of fibrosis and cirrhosis in up to 15% of patients. Insulin resistance is one of the most frequent findings associated with NAFLD, together with features of metabolic syndrome such as obesity, central fat distribution, diabetes, dyslipidemia, and atherosclerosis, assigning NAFLD as the hepatic manifestation of metabolic syndrome (Hardy, 2015; Foster, 2017). Dietary vitamin E is solubilized into mixed micelles in the intestinal lumen, absorbed in the small intestine via passive diffusion, and packaged into chylomicrons. A recent study, however, has suggested the role of scavenger receptor class B type 1 (SR-BI) in mediating vitamin E transport across the enterocytes (Reboul, 2015). On entry into the circulation via the lymphatic system, chylomicrons are hydrolyzed by lipoprotein lipase (LPL) and, as a result, a fractionof vitamin E is released and taken up by extra hepatic tissues via the postulated LPL-dependent bridging

mechanism (Rigotti, 2007). In clinical studies, metadoxine has been reported to scale back half-life of ethanol in healthy volunteers and in acutely intoxicated patients; to accelerate the metabolism of alcohol and acetaldehyde into less toxic higher ketones and to enhance their urinary clearance; to revive laboratory variables like alcohol, ammonia, γ-GT, and alanine aminotransferase; and to enhance clinical symptoms of alcohol intoxication, including psychomotor agitation, depression, aggressiveness, and equilibrium disorders (Addolorato, 2003; Addolorato, 2022) there's also evidence that metadoxine has an impact on reducing looking for alcohol (Yang, 2009) Data from clinical studies also support an impact of metadoxine on reducing indices of liver cell necrosis and fat accumulation in alcoholic liver disease (Yang, 2009) Metadoxine may block the differentiation step of pre-adipocytes by inhibiting CREB phosphorylation and binding to the c-AMP response element, thereby repressing CCAAT/enhancer- binding protein b during hormone-induced adipogenesis (Caballeria, 1998) Metadoxine, when given in an instantaneous release form in doses from 300 mg twice each day to 500 mg 3 times each day of up to three months, has been shown to enhance biochemical indices of liver function also as reduce ultrasonic evidence of liver disease disease (Cacciateore, 1998; Shenoy, 2014) Metadoxine may be a selective antagonist of the serotonin receptor subtype 5-HT2B and displays high affinity to the gamma- aminobutyric acid (GABA) transporter. In vitro enzymatic assay revealed that metadoxine reduced the activity of the GABA transaminase enzyme, liable for the degradation of GABA because it doesn't affect dopamine, norepinephrine or serotonin levels, metadoxine displays a completely unique mechanism of action as a monoamine-independent GABA modulator (Metadoxine extended release, 2014) the rise of carboxylic acid esters within the liver of ethanol-treated rats, prevented the formation of liver disease in rats exposed to a dose of ethanol sufficient to induce liver disease , increased glutathione levels within the hepatocytes of acutely and chronically alcohol-intoxicated rats, prevented glutathione depletion, lipid peroxidation damage, collagen deposition, and TNF-α secretions induced by alcohol and acetaldehyde in hepatocytes and hepatic stellate cells (Addolorato, 2003)

MATERIALS AND METHODS

Study design and site: This was a retrospective observational study in which all fatty liver patients at Santhiram Medical College & General Hospital, Nandyal, Kurnool Dist. Andhra Pradesh, India, had their history and laboratory findings checked. The research period extends from July-2018-Jan-2019. A retrospective comparative study is planned to conduct in gastroenterology department population. The patients was enrolled into the study only after the ultrasound scan of the liver, reports the fatty liver condition and the treatment was given for 3 months and prognosis is observed every month by ultrasound scan of the liver.

INCLUSION AND EXCLUSION CRITERIA: All patients diagnosed with fatty liver disease admitted/or present for consultation in the gastroenterology ward of SRGH, NANDYAL were enrolled during the study period. Patients either past history or early diagnosed with fatty liver are included in the study. Irrespective of age, gender, personal, occupational history and other complications or co morbidities are involved in to the study. Patients with poly pharmacy are involved in to the study. Patients with diagnosis of fatty liver and treatment with Vitamin-E supplements are involved in to the study.Patients with diagnosis of fatty liver and treatment with Metadoxine and L-Asparagine are involved in to the study and compared with the Vitamin-E supplements. In exclusion criteria pediatrics are not involved in the study. Patients diagnosed with grade-I fatty liver, steatohepatitis,and cirrhosis are excluded from the study. Patients prescribed with Vitamin-E, Metadoxine+L-Asparagine for other clinical conditions except faty liver are excluded from the study.

Data Collection Procedure and Data Analysis: Patient data collection form was developed based on essential details to be collected from the patient .Demographic information like name, age, sex, and locality were included. Parameters like description of pain, onset of pain, duration of pain, intensity of pain, were included. Diagnosis and treatment protocol were included. Ultrasound scan of the abdomen was done to know the status o the fatty liver. The data regarding the drugs that the physician has prescribed for particular patient individuals was collected.

Statistical Data Management and Analysis: The data was analyzed using paired T-test statistical software version 6.04 and SPSS (statistical package for social science) software version 22.0. Mean difference and P value for continuous variables and percentages for categorical variables are reported relevant.

RESULTS

A total of 110 cases of fatty liver were included in the study conductedduring the study period. Out of these 110 patients, 96 were males and 14 were females.Table-1 gives the information about gender wise distribution of fatty liver patients.

Table 1. Gender wise distribution of fatty liver patients

Gender	No. of patients	Percentage(%)
Males	96	87.3%
Females	14	12.7%
Total	110	100

Based on the gender wise distribution, the prevalence of fatty liver is seen more in male patients with 87.3% and less in female patients with 12.7% respectively.

Table 2. Age wise distribution of Fatty liver patients

Age	Males	Females	Total	%
18-28	8	0	8	7.3
29-38	19	8	27	24.8
39-48	25	3	28	25.7
49-58	32	2	34	31.2
59-68	8	0	8	7.3
69-78	0	0	4	3.7
79-88	4	0	0	0
89-98	0	0	0	0
TOTAL	96%	13	109	-
	88.1%	11.9%	-	P=NS

Based on age wise distribution, the highest prevalence rate is seen in patients with age group of 49-58 years with 31.8% respectively.

Table 3. Distribution of data based on personal history among males

MALES	ALCOHOLIC	NON ALCOHOLIC
96	73(76%)	23(26%)

Out of 96 patients (males), alcoholic patients are about 76% and non alcoholicpatients are about 24%.

Table 4. Distribution of patients based on stages of fatty liver

Totalnumber ofpatients	Grade-II fatty liver	Grade-III fatty liver
110	69(62.7%)	41(37.3%)

Out of 110 patients, the patients with Grade-II fatty liver are 62.7% and Grade-IIIfatty liver are 37.3%

Table 5. Distribution of drugs among fatty liver patients

Total numberofpatients	Vitamin-E	Metadoxine +L-Asparagine
110	55(50%)	55(50%)

The drugs Vitamin-E and Metadoxine +L-Asparagine were equally distributedamong the total number of patients.

Table 6. Distribution of drug (Vitamin-E) among grade-II and grade-III fattyliver patients

Drug name	Grade-II Fatty liver	Grade-III Fatty liver
Vitamin-E(55)	30(54.5%)	25(45.5%)

The drug Vitamin-E was given to the 55 patients, among them 30 patients are withgrade-II fatty liver and 25 patients are with grade-III fatty liver.

Table 6. Distribution of drug (Vitamin-E) among grade-II and grade-III fattyliver patients

Drug name	Grade-II Fatty liver	Grade-III Fatty liver
Vitamin-E(55)	30(54.5%)	25(45.5%)

The drug Vitamin-E was given to the 55 patients, among them 30 patients are withgrade-II fatty liver and 25 patients are with grade-III fatty liver.

Table 7 Distribution of drug (Metadoxine+ L-Asparagine) among grade-IIand grade-III fatty liver patients

Drug name	Grade-II Fatty liver	Grade-III Fatty liver
Metadoxine+ L-Asparagine(55)	30(54.5%)	25(45.5%)

The drug Metadoxine+ L-Asparagine was given to the 55 patients, among them 30patients are with grade-II Fatty liver and 25 patients are with Grade-III Fatty liver. After the treatment of fatty liver, the both drugs (Vitamin-E and Metadoxine +L-Asparagine) shows normal echogenecity.

DISCUSSION

In this study screening for fatty liver disease was conducted for 110 patients in Santhiram medical college and general hospital. In this study 110 subjects have been included, out of which about 87.3% were males and 12.7% were females. Table-1 concludes that the total of 110 cases of fatty liver was participated in the study. Out of these 110 patients, 96 were males and 14 were females. Males are more prone to fatty liver disease due to alcohol consumption and the females are diagnosed with fatty liver are due to obesity. From Table-2, it concludes that subjects of age 49-58 years are more prone to develop fatty liver disease, 31.8% cases of age 49-58 were diagnosed as Fatty liver disease. New cases were diagnosed at the age group of 18-28 years due to sedentary life style. Fatty Liver disease is commonly associated with age, obesity and hyperlipidemia .Most of our patients were in age group of 29-58 years. Table-3 concludes that among males i.e out of 96 patients, 73 patients develop fatty liver is due to alcohol consumption and the females are diagnosed with fatty liver are due to obesity and hyperlipidemia . In the alcoholic fatty liver disease, accumulation of fat in the liver is mainly due to excess alcoholic consumption. In the course of NAFLD, there are two important steps. The first step is characterized by lipid accumulation in the hepatocytes. In the second step, Steatohepatitis and oxidative stress is responsible for the hepatic inflammation and fibrosis. Table-4 concludes that out of 110 patients, the patients with grade-II fatty liver are 69(62.7%) and the patients with grade-III fatty liver are 41(37.3%). The grade-II fatty liver is mainly developed due to high fat consumption. The grade-III fatty liver is mainly due to the excess intake of alcohol, obesity and hyperlipdemia.

Table-5 concludes that the drugs Vitamin-E and Metadoxine + L-Asparagine were equally distributed among total subjects that were included in the study. Table-6 concludes that the drug Vitamin-E was given to the 55 patients, among them 30 patients are with grade-II Fatty liver and 25 patients are with grade-III fatty liver. Table-7 concludes that the drug Metadoxine +L-Asparagine was given to the 55 patients, among them 30 patients are with grade-II fatty liver and 25 patients are with grade-III fatty liver. Table-8 concludes that comparision of efficacy of Vitamin-E and Metadoxine+L-Asparagine in treating fatty liver was observed and both the drugs shows normal echogenicity on ultrasonography. Table-9 concludes that the treatment of fatty liver with Vitamin-E shows reduced size of the liver. Because as Vitamin-E is an anti-oxidant, it donates the hydrogen atom from its structure and neutralizes the free radical content in the liver. The Metadoxine plays an important role in the clearance of alcohol from the liver.

Table 8. Comparision of efficacy of Vitamin-E and Metadoxine +L-Asparagine in treating fatty liver

Parameter	Vitamin-E group		Metadoxine+L-Asparagine	
Echogenecity byultrasonography	Before treatment	After treatment	Before treatment	After treatment
Raised Echogenecity	55	00	55	00
Normal Echogenecity	00	55	00	55

Table 9. Mean difference and P value for the drugs (Vitamin-E and Metadoxine +L-Asparagine)

Parameter	Vitamin-E group			Metadoxine +L-Asparagine		
Size ofthe liver (cm).	Before treatment	After treatment	P-Value	Before treatment	After treatment	P-Value
Mean liver sizeon ultrasonography	14.42+1.29	13.6+87	<0.0001	13.51+1.15	13.51+1.15	NA
Mean differencein liver size	0.8+0.09		-	Nil		-

CONCLUSION

Fatty liver is a reversible condition in large vacuoles of triglycerides fat accumulates in the liver cells via the process of steatosis.It occurs in two forms they are alcoholic and non alcoholic fatty liver. Alcoholic fatty liver is a condition in which excess fat is stored in the liver due to heavy alcohol use. Non alcoholic fatty liver is a condition in which excess fat is stored in the liver. This accumulation of fat is not caused by heavy alcohol use.s Non alcoholic fatty liver disease(NAFLD) is rapidly becoming the most common liver disease worldwide. The prevalence of NAFLD is higher in general population of western countries is 20-30%.About 2-3% of the general population is estimated to have non-alcoholic steatohepatitis (NASH), which may progress to liver cirrhosis and hepatocarcinoma. The prevalence of NAFLD is higher in males and increases with age. Indians have higher prevalence of fatty liver than the Europeans. Almost one third of the urban population in india is suffering from fatty liver. The study was conducted for 110 study subjects.Out of which,96 patients ae males and 14 patients were females and the both the drugs were equally given to the total number of patients. The statistical methods were applied to the raw data and the results were carried out. Our study concludes that the treatment of fatty liver with vitamin-E is more effective when compared with the treatment of Metadoxine +L- Asparagine. Treatment with Vitamin-E costs less(25/- per 10 tablets) when compared with the treatment with Metadoxine +L-Asparagine(139/- per 10 tablets) and there are negligible side effects, In future our data must be confirmed in larger scale studies with pre and post treatment biopsies.

CONSENT: As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL: Ethical approval for this study was obtained from theInstitutional Ethical committee bearing no: IEC/2018/13.

COMPETING INTERESTS: Authors have declared that no competing interestsexist.

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